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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 20040224

Application Number: 08/160,965
Filing Date: December 02, 1993
Appellant(s): MUSSER ET AL.

James M. Musser, et al.
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed December 16, 2003.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that claims 1, 4-35 and 46-47 stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

No prior art is relied upon by the examiner in the rejection of the claims under appeal.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-35 and 46-47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an immunogenic composition and method of producing an immune response comprising a physiologically acceptable non-toxic vehicle containing a purified non-proteolytic streptococcal pyrogenic endotoxin B (SPEB), which produces an immune response in a mammal against Group A streptococcal infection wherein said SPEB comprises at least one amino acid substitution and said substitution occurs at the amino acid position selected from the group consisting of Lysine145, Glutamine185, Cysteine192, Histidine340, Asparagine356 and Tryptophan357.

The written description rejection is on the grounds that the claims and specification fail to recite the reference sequence from which the amino acid substitutions are drawn. The reference sequence from which the specific amino acid substitutions are drawn has not been disclosed; and therefore the written description is not commensurate in scope with the claims drawn to specific amino acid substitutions.

The instant specification fails to provide the identity of the entire SPEB sequence used in the composition or method of producing an immune response comprising using a cysteine protease comprising at least one amino acid substitution and said substitution occurs at positions 145, 185, 192, 340, 356 and 357. There is no description of the reference cysteine protease, neither do the claims recite the base sequence that is being substituted.

The instant specification repeatedly states that the previous known sequences are incorrect and that there are discrepancies between the instant sequence and other known sequences. At page 20, lines 2-6 the specification states that "The published amino acid sequence for cysteine protease, including the configuration of the presumed active site is incorrect. The predicted amino acid sequence encoded by this sequence is not cognate with the published cysteine protease sequence. Instead, the nucleotide sequence resembles, but is distinct from, the allele described by Hauser and Schlievert." Example 8 of the instant specification states "The speB gene (speB7) in strain MGAs 1719 does not encode a protein with the amino acid sequence presented previously. There are discrepancies between the protein sequence from strain B220 and a *speB* allele (herein designated *speB1*) in serotype M12 strain (86-858). The

specification is quite clear in stating the instant sequence is unlike the sequences known in the prior art. However, the specification fails to disclose what the identity of the reference sequence from which the amino acids substitutions is based upon. The specification is replete with statements that the prior art fails to teach the instant reference sequence. At page 32 lines 10-13 the specification states " Targets for functional amino acid replacement are based on biochemical analysis if cysteine protease (Tai, et al., 1976) and by analogy with similar residues in the eurkaryotic cysteine protease, papain (Kamphuis, et al., 1984)." However, the Tai et al., fails to teach the entire reference sequence. Moreover the sequence of Tai et al., fails to teach lysine at position 145 but rather an Arginine, a Glutamine at 185 but rather a Tyrosine, and a Cysteine at 192 but rather Valine. Furthermore the sequence of Tai et al., only shows an amino acid sequence through positions 252. And it is noted that this reference is not incorporated into the specification. Therefore, an analysis of the Tai et al., shows that the Tai et al., shows a completely different sequence making it doubtful that it contains the sequence from which the functional amino acid replacements are based upon. Without knowing the reference sequence, one cannot really know the significance of substituting amino acids at positions Lysine145, Glutamine185, Cysteine192, Histidine340, Asparagine356 and Tryptophan357.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The

specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of using. The reference sequence referred to is required. Thus a precise description of the reference sequence is necessary in order to determine the amino acids which can be substituted. Thus the specification is insufficient to support the instant claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645. The specification must set forth the precise invention for which a patent is solicited, in such manner as to distinguish it from other inventions and from what is old. It must also describe completely a specific embodiment. The instant specification fails to set forth the precise invention for which a patent is solicited because it fails to disclose the reference sequence from which the amino acid substitutions are drawn. Moreover, the specification fails to describe completely a specific embodiment; i.e., the reference sequence and the associated amino acid substitutions. The specification makes clear that the instant sequence is different from the prior art sequences, yet fails to disclose the identity of this sequence. The structure of reference sequence has not been defined or described by the instant specification.

In view of these considerations, a person skilled in the art would not have viewed the teachings of the specification sufficient to show that applicants were in possession of an immunogenic composition and method of producing an immune response

comprising a physiologically acceptable non-toxic vehicle containing a purified non-proteolytic streptococcal pyrogenic endotoxin B (SPEB), which produces an immune response in a mammal against Group A streptococcal infection wherein said SPEB comprises at least one amino acid substitution and said substitution occurs at the amino acid position selected from the group consisting of Lysine145, Glutamine185, Cysteine192, Histidine340, Asparagine356 and Tryptophan357 when the specification fails to disclose the reference sequence wherein the substitution can occur. immunogenic composition comprising the mutated cysteine protease and method of producing an immune response as asserted in the specification as instantly claimed.

(11) Response to Argument

Response to Arguments Traversing the Rejection of Claims 1, 4-35 and 46-47 under 35 U.S.C. 112, first paragraph

Appellants assert that the Office failed to understand the invention is not the SPEB sequence itself but the substitutions at specific locations with the known and old sequence given that the Office presumes that the full sequence from which the specific amino acid substitutions are drawn is required for the written description to be commensurate in scope with the claims drawn to specific amino acid substitutions.

However, contrary to appellants' belief that the Office misunderstood the invention; the Office clearly understands appellants' proposed invention. The Office understands the concept of specific amino acid substitutions within an amino acid sequence, however because appellants failed to disclose what specific sequence is

"known and old" the Office can not determine what specific amino acid sequence can tolerate the claimed amino acid substitutions. Therefore, the office deems that the specification lacks sufficient written description. The also Office understands that contrary to appellants assertion that the sequence is "known and old" appellants' own specification that the known and old sequences of the prior art are incorrect. Therefore, appellant's instant arguments are not commensurate with the statements in the instant specification, especially when the instant specification states that the predicted amino acid sequence encoded by this sequence is not cognate with the published cysteine protease sequence.

Appellants assert that the skilled artisan for this particular art would recognize that the invention had possession the invention at the time of filing because the native speB sequence was in the public domain. However, if the skilled artisan read appellants specification, they would read that appellant claims the instant specification repeatedly states that the previous known sequences are incorrect; distinct and contain discrepancies between the instant sequence and other known sequences making the predicted amino acid sequence encoded by this sequence is not cognate with the published cysteine protease sequence. See pages 20, lines 2-6, and page 24, line 9-12. Then a skilled artisan would read at page 32 that targets for functional amino acid replacement are based on biochemical analysis if cysteine protease (Tai, et al., 1976) only to realize that Tai et al., fail to teach: the entire reference sequence; a sequence containing the wild-type speB sequence having the claimed residues at positions Lysine at 145, Glutamine185, Cysteine192; and a sequence containing any amino acid at

positions 340, 356 and 357. Therefore, if this reference sequence "known and old" in the art, it is curious why appellants have failed, even now to disclose it.

Appellants point to pages 22-23 lines 4-2 as support for providing to a skilled artisan sufficient knowledge thereby obviating the need to disclose the readily available "known and old" *speB* sequence. However the passage states that the gene was amplified by polymerase chain methods (PCR); amplification is a molecular cloning technique that allows for the amplification of specific DNA it is not a substitute for sequence analysis. The example further states that the gene was amplified with oligonucleotide primers and recites specific amplification reagents and techniques. The disclosed primer sequences teach the sequence used to initiate replication. There is no teaching of the identity of the wild-type reference sequence. Appellants' support fails to show the structure of the readily known and old sequence. Appellants' support fails to even show what basis in the prior art for appellants' assertion of the knowledge of a readily known and old sequence. Appellants do not incorporate by reference a particular sequence known in the art. Therefore, appellants' fails to show sufficient support.

Appellant asserts that inventors own article (Kapur, 1993) reported the methodical and prolific sequence of 39 SPEB alleles and identified that alleles differ in sequence from one another at only one or two amino acids that are clustered in a ten amino acid region. The alleles differing at one or two positions within a ten amino acid region does not teach the wild-type sequence. Appellants appear to be stating that in every ten amino acids one or two amino acids can vary, and that if there are at least

357 amino acids and in each group of ten one or two amino acids vary then the protein that each produces allows for a great deal of variation. Furthermore, the article states that three different proteases are encoded. Different amino acid sequences encode different proteases. Thus, the Kapur et al., reference does not clarify the identity of the reference sequence, rather just the opposite since the article states that different amino acid sequences encoded different proteases. Appellants fails to state which amino acid sequence referred to by Kapur et al., is the reference amino acid sequence used as the basis for the instant claims. The Kapur et al., article fails to disclose the sequence of a sequence containing the at least 357 amino acid sequence which can be substituted. Moreover, Figure 3 only the amino acid similarities within a ten-amino acid region; it does not disclose the reference sequence. Moreover, the materials and methods section fails to describe any sequence procedures. Rather the section entitled Sequencing of the cysteine protease structural gene teaches that the gene was amplified by PCR and as discussed above amplification of specific DNA it is not equivalent for sequence analysis.

Appellants assert that Figure 3 divulges that because GenBank accession numbers are provided for the 38 different sequences, the appellants do not need to disclose the reference sequence. Figure 3 shows different nucleotides within the amino acid region of 308-317 according to appellants. The instant claims do not comprise of an amino acid substitution within the range, therefore it is impossible to distinguish which allele is the wild type being referenced by the claims. Figure 3 does not disclose the wild type sequence which has a Lysine145, Glutamine185, Cysteine192,

Histidine340, Asparagine356 and Tryptophan357. Neither does figure 3 state which of the 38 alleles has a sequence that can tolerate substitutions at Lysine145, Glutamine185, Cysteine192, Histidine340, Asparagine356 and Tryptophan357. The figure fails to even disclose which of the 38 alleles produces what mature protease. And the article does not state that the entire wild-type sequence of the 38 alleles is completely identical except for the amino acids the ten amino acid region. The specification fails to incorporate the article into specification and the specification fails to stated which allele has a Lysine145, Glutamine185, Cysteine192, Histidine340, Asparagine356 and Tryptophan357. The fact that GenBank contains sequences of SPEB alleles does not obviate the instant issue of the identity of a wild-type sequence that comprises Lysine145, Glutamine185, Cysteine192, Histidine340, Asparagine356 and Tryptophan357. Moreover, the instant specification fails to disclose any of the arguments appellants' presents as being drawn to the Kapur et al. article.

Appellants than site *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d at 1384, 231 USPQ at 94 as support for what is conventional or well known to a skilled artisan need not be disclosed in detail. However, appellant's specification fails to disclose what is well known. Outside of appellants' instant assertions, the specification teaches the sequence previously known in the art to encode the protease is incorrect. The instant specification also states that the undisclosed sequence of the instant application encodes a different protease than the ones known in the prior art. And the instant specification teaches a variety of sequence discrepancies among the alleles. Therefore, the instant specification fails to rely on conventional and well-known art, in

view of its recitation that the conventional and well-known art is incorrect. Furthermore, the written description rejection does not require a detailed description; rather the rejection is because there is no description of what the wild type sequence proposed by appellants.

Appellants state that the reference sequence used to generate the instant claims was in the public domain prior to the time of filing and is therefore not required. However, appellants continuously fail to point to the specific sequence that is allegedly in the prior art. Moreover, the fact that reference sequence that generated the invention of instant claims was available, but not make the sequence of the instant invention known when appellants fail to disclose the specific reference sequence used to generate in instant claims. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996). Since the level of knowledge in the art would not permit on skilled in the art to immediately envisage the product claimed in view of the fact the prior art sequences were incorrect and contain many discrepancies, appellants arguments fail to be persuasive.

Appellants state the it is well settled in case law that in claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass and that such a formula is normally an adequate description of the claimed genus. Here, applicants fail to disclose the "formula" or wild-type amino acid sequence

from which specific substitutions are made. The specification teaches that the prior art sequences art incorrect and that there are amino acid differences between the alleles. Appellant has failed to disclose in the instant specification a generic wild-type sequence. Moreover, the instant application refers to a proposed sequence. Thus, appellant cannot rely on what is known in the art if appellants specification discloses that what was known in the art is incorrect. Appellants point to page 7, lines 4-5 that says the cysteine protease is a translated portion of the SPE B gene or fragments or derivatives thereof.

There is no disclosure of a wild-type amino acid structure. There is no disclosure saying the translated portion of the SPE B gene or fragments or derivatives thereof can tolerate substitutions at the Lysine145, Glutamine185, Cysteine192, Histidine340, Asparagine356 and Tryptophan357. The definite of the cysteine protease fails to identify the missing information. Moreover, the details of the specific mutations that impart the non-proteolytic characteristics being provided for at page 32 is not at issue; rather the issue is what the wild-type sequence that can tolerate amino acid substitutions at position Lysine145, Glutamine185, Cysteine192, Histidine340, Asparagine356 and Tryptophan357 to create a non-proteolytic protease. Appellants' fail to disclose what the reference sequence is.

Appellant assert that page 19, line 21 provides a sequence corresponding to amino acids 146-156 as a common structure to *speB* and its variants. However disclose of amino acids 146-156 does not teach the full reference sequence. The lack of disclosure makes it impossible to determine the full sequence of over 357 amino

acids based on 10 amino acids. Moreover, Figure 1 is SDS-PAGE gel electrophoresis which compares molecular weights. It does not teach a sequence by which one can compare the substitutable amino acid positions. Appellants assert that the description of structural features were provided, however contrary to appellants belief SDS-PAGE results do not teach the structural identity of the wild-type sequence. Amino acids 146-156 do not teach of the entire wild type sequence. The skilled artisan cannot envision the detailed structure of the isolated protease, thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. An adequate description requires more than a mere statement that it is part of the invention. The wild-type amino acid sequence itself, or a nucleic acid structure is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Appellants assert that *Lockwood v. American Airlines, Inc.*, 41 USPQ2d 1961, 1964-65 (Fed. Cir. 1997) antibody cross-reactivity may be sufficient to show possession. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.,* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). For some biomolecules, examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight, and length. Although structural formulas provide a convenient method of demonstrating possession of specific molecules, other identifying characteristics or combinations of characteristics

may demonstrate the requisite possession. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Regents of the University of California v. Eli Lilly,* 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997); *Amgen, Inc. v. Chugai Pharmaceutical,* 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it"). The instant specification does not describe the claimed invention sufficient to show that the applicant was in possession of the claimed invention. Appellant have failed to show the structure, a drawing, diagram, formula of the reference sequence, a sequence, binding affinity, binding specificity or the like.

The *Lockwood* court stated the antibody cross-reactivity "may" be sufficient; however, in this case, the antibody cross-reactivity can not be deemed sufficient when appellants own work shows the uncertainty within the art. Cross-reactivity only shows that there are common epitopes, cross-reactivity does not provide any disclosure as to the sequence of the reference sequence. Neither does cross reactivity teach what sequences can tolerate the substitutions proposed in the instant claims. Therefore, appellants fail to be sufficient to overcome the written description rejection.

Compliance with the written description requirement is essentially a fact-based inquiry that will necessarily vary depending on the nature of the invention claimed. '" *Enzo Biochem*, 296 F.3d at 1324, 63 USPQ2d at 1613. In this case, the prior art sequence is incorrect, several different proteases can be encoded based on a variety of different amino acid sequences and appellant has fail to show a wild-type sequence comprising Lysine145, Glutamine185, Cysteine192, Histidine340, Asparagine356 and Tryptophan357. Therefore, appellants' assertion fails to be persuasive.

Appellant assert that they were in possession of SPEB that can be used in an immunological composition. However the issue is not whether the composition has immunogenic properties but rather what is the structural identity of the SPEB used to a the basis for the amino acid substitutions. The art and specification teach that there are different alleles having different sequences; different amino acid sequence encode different proteins; yet what appellant fail to teach is which sequence comprises Lysine145, Glutamine185, Cysteine192, Histidine340, Asparagine356 and Tryptophan357.

Contrary to appellants' assertion that purification provided by the specification is sufficient to provide written description, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. An adequate description requires more than a mere statement that it is part of the invention. The wild-type amino acid sequence itself, is required and appellants have failed to provide such. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Appellant asserts that possession may be shown in a variety of ways that provide distinguishing characteristics. See *Enzo Biochem*, 296 F.3d at 1326, 63 USPQ2d at 1614 ("reference in the specification to a deposit may also satisfy the written description requirement with respect to a claimed material") but appellants failed to do such. The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art. Appellants assert that they have a sequence, which is unlike the incorrect sequences of the prior art that encodes a protein not known in the prior art; yet appellants fail to disclose this sequence. A lack of adequate written description issue arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product or if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. The instant application fails to provide the identity of the wild-type sequence for which the amino acid substitutions are drawn to.

Appellants assert that they meet the standards under *Eli Lilly*. However, for the written description requirement, an applicant's specification must reasonably convey to those skilled in the art that the applicant was in possession of the claimed invention as of the date of invention. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997); *Hyatt v. Boone*, 146 F.3d 1348, 1354, 47 USPQ2d 1128, 1132 (Fed. Cir. 1998). However, at the date the invention appellants' only conveyed to those skilled in the art that the prior art was

wrong and that appellants encoded a protein different from the prior art. The appellants did not disclose what the sequence is; what the numbering system used to determine the amino acid positions is based upon, nor did appellants provide the full sequence identity of an immunogenic composition and method of producing an immune response comprising a physiologically acceptable non-toxic vehicle containing a purified non-proteolytic streptococcal pyrogenic endotoxin B (SPEB), which produces an immune response in a mammal against Group A streptococcal infection wherein said SPEB comprises at least one amino acid substitution and said substitution occurs at the amino acid position selected from the group consisting of Lysine145, Glutamine185, Cysteine192, Histidine340, Asparagine356 and Tryptophan357.

Appellants urge that the disclosure teaches the invention of mutated SPEB residues because the reference SPEB sequence itself was known. Again, appellant state that the reference sequence was known, yet appellant fail to precisely point out even in the prior art a precise reference sequence; moreover appellants fail to point out a reference sequence SPEB, from which the substitutions comprising at least one amino acid substitution and said substitution occurs at the amino acid position selected from the group consisting of Lysine145, Glutamine185, Cysteine192, Histidine340, Asparagine356 and Tryptophan357 are based.

Appellants point to the specification for the teaching of the generation of mutant *speB* proteins saying that mutations are based upon old and well-known methods. Again, appellants misquote the reasons for the rejection. Whether or not mutation techniques are old and well known in the art is not the issue; the issue is what is the

wild-type sequence that tolerates amino acid substitutions at position Lysine145, Glutamine185, Cysteine192, Histidine340, Asparagine356 and Tryptophan357 to create a non-proteolytic protease. Appellants' fail to disclose what the reference sequence, therefore appellants have not adequate described in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Appellants assert that the specification provides evidence that appellant had possession. Appellant points to pages 22-23 as support. However the passage states that the gene was amplified by polymerase chain methods (PCR); amplification is not a substitute for sequence analysis. The example further states that the gene was amplified with oligonucleotide primers and recites specific amplification reagents and techniques. The recitations of primer sequences fail to teach the identity of the reference sequence from which the instant claims are drawn. There is no teaching of the identity of the wild-type reference sequence. Appellants' show no structure that is readily known and old in the art as the reference sequence. Appellants' fails to show what basis in the prior art for appellants' assertion of the knowledge of a readily known and old sequence. Appellants do not incorporate by reference a particular sequence known in the art.

Then appellants' state that "PCR was clearly not performed without knowledge of the sequence"; yet the specification fails to disclose any type of sequence analysis on the reference strain. Therefore, appellant assertion that PCR was not performed without the knowledge of the DNA sequence is unpersuasive. Moreover, appellants only had a

predicted amino acid sequence that was not cognate with the published cysteine protease sequence. There's no evidence that appellant found the sequence of the predicted structure. At best, there is evidence of the sequence of prior art sequences, however appellants state that those sequences are incorrect. It is while known that a complete specification, should include the detailed description of the invention, any specific embodiments that have been disclosed, the claims and any specific, substantial, and credible utilities that have been asserted for the invention. Here, the specification lacks any reference to the performance of any sequence analysis. Moreover, the inventor in his 1993 article Kapur et al., lacks any disclosure of sequence analysis. Thus, the argument that PCR was clearly not performed without knowledge of the sequence is unpersuasive since there is absolutely no data within the specification stating that sequence analysis was performed.

Appellants again state that site-directed mutagenesis described in the specification clearly illustrate that the inventors knew the identity of the sequence being mutated. However, mutagenesis fails to provide the identity of the sequence being mutated to those skilled in the art because the specification fails to describe in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Appellant asserts that a skilled artisan would know the significance of the particular substitution. However the issue is not whether a skilled artisan would know the significance of the particular substitution. The reference to specific amino acid positions without a base sequence to compare when the instant specification fails to

provide the structure of the base sequence is the issue. The issue can also be characterized by asking whether at the time the application was filed, had possession of the claimed invention drawn to an immunogenic composition and method of producing an immune response comprising a physiologically acceptable non-toxic vehicle containing a purified non-proteolytic streptococcal pyrogenic endotoxin B (SPEB), which produces an immune response in a mammal against Group A streptococcal infection wherein said SPEB comprises at least one amino acid substitution and said substitution occurs at the amino acid position selected from the group consisting of Lysine145, Glutamine185, Cysteine192, Histidine340, Asparagine356 and Tryptophan357 that was described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors and the answer is no. It is appellant responsibility to fully and adequately disclose essential subject matter in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor invented. Appellant failed to describes and disclose the sequence from which the amino acid substitutions are based.

In summary, Appellants failed to point to one piece of art that contained a sequence that is allegedly "known and old" in the art. Nowhere in the specification, does it state that the reference sequence is well known in the art, rather the appellants have asserted this belief without any support from the specification. Moreover, while appellants' argue that the sequence is old and well known in the art, appellants' own instant specification states the opposite, that the prior art sequences are incorrect and

that the sequences comprises variability. In view of variability between alleles one skilled in the art needs to the exact sequence which can be mutated, yet appellants failed to disclose that data. Appellants' arguments that PCR and mutagenesis clearly illustrate that the inventors knew the sequence is wholly insufficient, because the performance of these techniques in no way defines or discloses what the reference amino acid sequence is. The art and instant specification teach that different amino acid sequences produce different proteases and the instant application produced a protease unlike the ones known in the art, therefore a skilled artisan would be needs to know the reference from which appellants, invention is based. The examiner has shown that the preponderance of the evidence shows why a skilled artisan would not recognize appellants' disclosure as being satisfactorily described since appellants failed to actually disclose the invention. Accordingly, appellant's arguments are not persuasive.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Ja-Na Hines
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